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14. ABSTRACT

The major hypothesis is that prior occupational exposure to polychlorinated biphenyls (PCBs) results in decrements in neuropsychological and neurological performance and the number of dopamine (DA) terminals in the basal ganglia determined by β-CIT SPECT imaging. At the conclusion of data collection 241 former capacitor workers have completed neuropsychological and neurological examinations, a comprehensive questionnaire, a blood draw to measure serum PCB and thyroid hormone concentrations, and a non-invasive test to determine bone-lead concentrations. This latter measure will allow us to control for exposure to lead--a potential confounder. 89 subjects have undergone brain imaging at the Institute for Neurodegenerative Disorders in New Haven, CT to determine the relationship between serum PCBs and the number of basal ganglia DA terminals. Serum PCB concentrations have been determined at Mt. Sinai School of Medicine and thyroid hormone concentrations have been determined at the Wadsworth Center. All data collection is complete; data analysis and manuscript preparation continues. Secure electronic databases have been created for all data.

15. SUBJECT TERMS
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INTRODUCTION

The major hypotheses to be tested in this project are that high-level occupational exposure of former capacitor workers to polychlorinated biphenyls (PCBs) will result in reductions in: (i) performance on neuropsychological and neurological tests that reflect the historic PCB body burden of the individual and (ii) the number of dopamine (DA) terminals in the basal ganglia.

Aging former capacitor workers, previously employed at capacitor manufacturing facilities located approximately fifty miles north of Albany, NY; underwent neuropsychological and neurological exams; completed a comprehensive occupational, residential and dietary questionnaire; had blood drawn to measure serum thyroid hormone and PCB concentrations, and underwent a non-invasive test to determine bone lead concentrations in Albany, NY. This latter measure will reduce the likelihood of confounding the neurological effects of prior PCB exposure with the neurological effects of prior lead exposure. Finally, approximately 40% of the subjects participated in a second portion of the study that used brain β-CIT SPECT imaging to determine whether prior occupational exposure to PCBs reduces the number of basal ganglia DA terminals. Imaging took place at the Institute for Neurodegenerative Disorders in New Haven, CT under the supervision of Dr. Kenneth Marek.

Results, obtained using β-CIT SPECT imaging, demonstrate a significant negative relationship between current serum PCB concentrations and decreases in the density of β-CIT binding only in women. These findings are supported by epidemiological data demonstrating increased Parkinson's disease mortality, again only in women (Steenland *et al.*, *Epidemiology* **17**(1), 8-13, 2006)

STUDY INVESTIGATORS

Albany, NY Based Testing

Richard F. Seegal - Wadsworth Center, New York Sate Dept. of Health (NYSDOH): Principal Investigator

Edward F. Fitzgerald - University at Albany, School of Public Health: Epidemiologist

Lenore J. Gensburg - University at Albany, School of Public Health: Tracing, Screening, Residential, Occupational, Dietary and Medical Histories

Eric S. Molho, Donald S. Higgins - Albany Medical Center: Neurological Assessment

Stewart A. Factor - Emory University: Neurology Consultant

Robert J. McCaffrey - University at Albany: Neuropsychological Assessment

Richard F. Haase - University at Albany: Biostatistician

Mary S. Wolff - Mount Sinai School of Medicine: Serum PCB Analyses

Andrew C. Todd - Mount Sinai School of Medicine: Bone Lead Determination

Patrick Parsons - Wadsworth Center, NYSDOH: Bone Lead Determination

New Haven, CT Based Testing

Kenneth Marek, John P. Seibyl, Danna Jennings - Institute for Neurodegenerative Disorders: ß-CIT SPECT Brain Imaging

PROGRESS IN FISCAL YEAR 2007

The following narrative details the progress we have made in the ongoing data analysis during the sixth year of the project. Data collection ended during the previous reporting period. We also provide in the narrative a table of the final tracing, screening and participation rates (see Table I). At the conclusion of data collection in April 2006 we had tested 241 subjects in Albany which represents 97% of our projected goal of testing 248 subjects. In addition, 89 of those subjects traveled to New Haven, CT to undergo β-CIT imaging to estimate the density of basal ganglia dopamine transporters. This number represents 93% of our stated goal of testing 96 subjects.

Significant effort has been made, and continues to be made, to analyze the vast amounts of data that were generated during active data collection. In addition to collecting the major dependent variables (neurological, neuropsychological, β-CIT, bone lead, thyroid hormone and serum PCB concentrations) we also collected extensive information from a 2-2.5 hour interview on potential confounders that may influence the dependent variable outcomes listed above. Interview data pertaining to demographic characteristics, medical history, medication use, smoking and alcohol consumption and diet (including consumption of sport-caught fish) and other relevant variables have been double data entered and subdivided into subject-specific SAS datasets. Edit programs have been developed to detect out-of-range and logical inconsistencies and any errors have been corrected. The occupational histories have been reviewed by two certified industrial hygienists who evaluated each job for the likelihood of exposure to PCBs, lead, mercury, and pesticides, using a four point scale. Each job has also been classified using Standard Industrial and Occupation codes and medications have been coded according to the American Hospital Formulary Service.

Table I. Tracing, screening and participation outcomes among former GE capacitor factory workers from Fort Edward and Hudson Falls, New York (N=2,844)

Tracing Outcome	**N**	**%**
Eligible for screening	1,124	39.52
Not eligible for screening		
Living	256	9.00
Dead	844	29.68
Unlocatable	577	20.29
End of study	43	1.51
Screening Outcome	**N**	%
Eligible for participation	484	43.06
Not eligible for participation		
Medically ineligible	348	30.96
Other ineligible	50	4.45
Refused		
After screening interview	110	9.79
Refused screening interview	42	3.74
Passively	80	7.12
End of study	10	0.89
Participation Outcomes	**N**	**%**
Participation in Albany, NY Portion of Study	241	49.79
Participation in New Haven, CT Portion of Study	89	36.93

Table II describes the demographic and background characteristics of the study participants. Out of a total of 241 participants, 129 (53.5%) were men and 112 (46.5%) were women. The mean age of the participants was 64.4 years, with a range from 50 to 87. There were no significant differences in mean age between the men (64.1 years) and the women (64.7 years).

Table II. Demographic and background characteristics of study participants (N=241)

Characteristic	**N**[§]	**% or Mean (SD)**
Gender		
Male	129	53.5
Female	112	46.5
Income ***		
=<15,000	20	9.0
15,000-30,000	50	22.4
30,000-45,000	59	26.5
45,000-60,000	42	18.8
60,000-75,000	29	13.0
=>75,000)	23	10.3
Marital status ***		
Married or live with partner	165	70.5
Divorced, never married, separated, or widowed	69	29.5
Lost weight in past year ***		
No	189	80.8
Yes	45	19.2
Had hepatitis or cirrhosis of the liver ***		
No	225	97.0
Yes	7	3.0
Age (years)		
Male	129	64.1 (8.1)
Female	112	64.7 (9.3)
Education (school years completed) **		
Male	122	13.1 (2.2)
Female	112	12.0 (1.7)
Body Mass Index (BMI, kg/m^2)		
Male	122	29.1 (4.5)
Female	111	30.0 (6.2)
Number of cigarette packs in the previous year		
Male	122	38.4 (111.4)
Female	112	46.6 (122.8)
Number of cigarette packs in the last 10 years		
Male	122	630 (1404)
Female	112	867 (1946)
Total number of drinks per week in the last year ***		
Male	122	6.84 (9.16)
Female	112	1.47 (3.46)
Total number of drinks per week in the last 10 years ***		
Male	122	7.01 (9.38)
Female	112	1.14 (2.62)
Number of births	112	2.71 (1.63)
Total weeks lifetime breastfeeding	112	7.18 (22.73)

[§] Number of observations varies across characteristics due to missing values
* The T-test or ChiSq is significant at p-value<0.05; ** The T-test or ChiSq is significant at p-value<0.01
*** The T-test or ChiSq test is significant at p-value<0.001

Table III lists current serum PCB concentration for all study participants expressed on a wet weight basis and lipid adjusted basis for individual PCB congeners as well as totals for light and heavy PCB congeners (defined as eluting before or after DDE (dichlorodiphenyldichloro-ethylene)) respectively. The geometric mean total serum PCB concentration for all subjects was 6.65 ppb on wet weight basis and 1.02 ppm on a lipid-adjusted basis; 7.47 ppb and 1.19 ppm for males, and 5.81 ppb and 0.86 ppm for females expressed on a wet weight and lipid adjusted basis respectively (data not shown). Congeners that are markers for occupational exposure include PCB-28, PCB-74, PCB-118, PCB-105 and PCB-156 and are identified below. After more than 30 years mean PCB levels are approximately three-fold higher in these former capacitor workers than in individuals of similar age who resided in the same towns but did not work at GE.

Table III. Current serum PCB concentrations of all study participants (N=241)

1980 BZ number	IUPAC number	IUPAC Structure	% of non-detectable or zero values	Wet Weight (ppb)			Lipid-basis (ppm)		
				Geometric Mean	Mean	SD	Geometric Mean	Mean	SD
Light PCBs [§]				**2.57**	**4.55**	**6.91**	**0.40**	**0.75**	**1.26**
28 [¥]	PCB-28	2,4,4'	20.3	0.09	0.43	1.11	0.01	0.07	0.19
74 [¥]	PCB-74	2,4,4',5	3.30	0.76	2.74	5.70	0.12	0.45	1.03
66	PCB-66	2,3',4,4'	14.1	0.17	0.40	0.34	0.03	0.06	0.06
56	PCB-56	2,3,3',4'	13.7	0.10	0.19	0.23	0.02	0.03	0.04
101	PCB-101	2,2',4,5,5'	4.10	0.27	0.48	0.42	0.04	0.08	0.07
99	PCB-99	2,2',4,4',5	5.00	0.15	0.32	0.43	0.02	0.05	0.08
Heavy PCBs [#]				**3.66**	**5.10**	**7.53**	**0.56**	**0.84**	**1.43**
118 [¥]	PCB-118	2,3',4,4',5	6.20	0.19	0.48	0.91	0.03	0.08	0.18
146	PCB-146	2,2',3,4',5,5'	3.30	0.07	0.14	0.28	0.01	0.02	0.05
153	PCB-153	2,2',4,4',5,5'	0.00	0.81	1.16	1.82	0.12	0.19	0.34
105 [¥]	PCB-105	2,3,3',4,4'	12.9	0.04	0.14	0.19	0.01	0.02	0.04
138	PCB-138	2,2',3,4,4',5'	0.80	0.63	1.04	1.92	0.10	0.17	0.37
178	PCB-178	2,2',3,3',5,5',6	9.10	0.03	0.08	0.09	0.005	0.01	0.02
187	PCB-187	2,2',3,4',5,5',6	2.10	0.13	0.19	0.21	0.02	0.03	0.04
183	PCB-183	2,2',3,4,4',5',6	3.30	0.06	0.08	0.06	0.01	0.01	0.01
167	PCB-167	2,3',4,4',5,5'	15.4	0.03	0.07	0.11	0.004	0.01	0.02
174	PCB-174	2,2',3,3',4,5,6'	5.00	0.05	0.07	0.05	0.01	0.01	0.01
177	PCB-177	2,2',3,3',4,5',6'	10.4	0.04	0.08	0.07	0.01	0.01	0.01
156 [¥]	PCB-156	2,3,3',4,4',5	4.60	0.15	0.33	0.74	0.02	0.05	0.14
172	PCB-172	2,2',3,3',4,5,5'	9.10	0.06	0.09	0.09	0.01	0.02	0.02
180	PCB-180	2,2',3,4,4',5,5'	0.40	0.44	0.63	0.96	0.07	0.10	0.17
170	PCB-170	2,2',3,3',4,4',5	1.20	0.19	0.30	0.50	0.03	0.05	0.09
201	PCB-199	2,2',3,3',4,5,5',6'	0.00	0.10	0.13	0.14	0.01	0.02	0.02
203	PCB-203	2,2',3,4,4',5,5',6	0.40	0.09	0.11	0.10	0.01	0.02	0.02
Total PCBs				**6.65**	**9.65**	**13.22**	**1.02**	**1.58**	**2.48**

[§] Elutes before DDE; [#] Elutes after DDE; [¥] Markers for occupational exposure

Table IV presents the relationship of current serum PCB concentrations (log adjusted, lipid basis) with key characteristics of study participants. Age was the demographic variable most strongly associated with log serum total PCB concentrations ($\beta = 0.015$, $p < 0.001$). Total PCB concentrations were higher among men than women ($\beta = 0.176$, $p < 0.001$) and among persons with less education ($\beta = -0.022$, $p = 0.041$). BMI was positively related to log serum PCB concentrations, but this association was statistically significant only for the light congeners ($\beta = 0.012$, $p = 0.032$).

Table IV. Multiple regression analysis of current serum PCB concentration (log adjusted, lipid basis) on demographic and background characteristics (N=233)

Characteristics of study participants	Serum PCB concentration (ppm)								
	Light PCBs[§]			Heavy PCBs[#]			Total PCBs		
	β	p-value	R^2	β	p-value	R^2	β	p-value	R^2
Age (years)	0.009	***0.009***	0.03	0.019	***0.0001***	0.25	0.015	***0.0001***	0.15
Gender (male)	0.156	***0.009***	0.03	0.168	***0.0001***	0.08	0.176	***0.0001***	0.07
Education (school years completed)	-0.031	***0.032***	0.02	-0.017	0.060	0.02	-0.022	***0.041***	0.02
BMI (kg/m^2)	0.012	***0.032***	0.02	0.002	0.577	0.00	0.007	0.090	0.01

[§] Elute before DDE: PCB-28, PCB-74, PCB-66, PCB-56, PCB-101, PCB-99
[#] Elute after DDE: PCB-118, PCB-146, PCB-153, PCB-105, PCB-138, PCB-178, PCB-187, PCB-183, PCB-167, PCB-174, PCB-177, PCB-156, PCB-172, PCB-180, PCB-170, PCB-201, PCB-203

Table V demonstrates that total cumulative occupational exposure to PCBs was significantly and positively associated with log serum total PCB concentration (log adjusted, on a lipid basis) after adjustment for age, gender, education, and BMI ($\beta = 0.056$, $p < 0.001$). This association was strongest in magnitude for the occupational light congeners, especially PCB-74 ($R^2 = 0.16$). Although some heavy congeners such as PCB-105 and PCB-156 were also statistically significant, in general the associations for the occupational heavy congeners were weaker in magnitude than those for the occupational light congeners. Cumulative exposure during the years that Aroclor 1016 was used was the exposure metric most strongly related to the occupational light congeners, particularly PCB-74 ($\beta = 0.249$, $p < 0.001$, $R^2 = 0.17$), although two heavy occupational congeners (PCB-105 and PCB-118) were also significant. In contrast, the strength of the association between log serum PCB levels and cumulative occupational exposure during the years that Aroclor 1242 was used was similar for both the occupational light ($\beta = 0.056$, $p < 0.001$, $R^2 = 0.09$) and occupational heavy congeners ($\beta = 0.032$, $p < 0.001$, $R^2 = 0.07$). These findings reflect the congener makeup of the Aroclors used during select periods of time. Occupational exposure to Aroclor 1254 was significantly associated with only one congener (PCB-156), a finding that may reflect the fact that only 10% of the study population was occupationally exposed to Aroclor 1254.

Table V. Multiple regression analysis of current serum PCB concentration (log adjusted, lipid basis) on cumulative occupational exposure to PCBs[Π], by Aroclor (N=233)

Serum PCB Concentration (ppm)	Cumulative exposure to PCBs							
	Aroclor 1254 (Years of use: 1946-1953)		**Aroclor 1242** (Years of use: 1954-1972)		**Aroclor 1016** (Years of use: 1973-1977)		**Total** (Years of use: 1946-1977)	
	β[¥]	**R^2**	**β[¥]**	**R^2**	**β[¥]**	**R^2**	**β[¥]**	**R^2**
Light PCBs[§]	-0.014	0.03	***0.044******	0.10	***0.041******	0.07	***0.082 *****	0.09
Occupational Light PCBs	-0.016	0.00	***0.056******	0.09	***0.078******	0.15	***0.144******	0.15
PCB-28	0.005	0.00	0.083	0.01	0.063	0.01	0.104	0.00
PCB-74	-0.053	0.00	***0.146******	0.07	***0.249******	0.17	***0.432******	0.16
Non-Occupational Light PCBs	0.015	0.00	***0.054****	0.03	0.002	0.00	0.040	0.00
Heavy PCBs[#]	0.018	0.00	***0.022******	0.06	0.012	0.02	***0.037****	0.05
Occupational Heavy PCBs	0.021	0.00	***0.032******	0.07	***0.027****	0.04	***0.060******	0.06
PCB-105	-0.093	0.00	***0.151****	0.05	***0.152****	0.04	***0.278****	0.04
PCB-118	-0.122	0.00	***0.100****	0.04	***0.085****	0.02	0.112	0.01
PCB-156	***0.177****	0.02	0.048	0.02	0.019	0.00	***0.126****	0.03
Non-Occupational Heavy PCBs	0.045	0.00	***0.043******	0.05	0.019	0.01	***0.071****	0.03
Total PCBs	0.009	0.00	***0.030******	0.08	***0.023****	0.04	***0.056******	0.08

[Π] Based on industrial hygienist assessment and years on job
* p-value<0.05; ** p-value<0.01; ***p-value<0.001
[¥] Adjusted for age, gender, education, and BMI
[§] Elute before DDE: PCB-28, PCB-74, PCB-66, PCB-56, PCB-101, PCB-99
[#] Elute after DDE: PCB-118, PCB-146, PCB-153, PCB-105, PCB-138, PCB-178, PCB-187, PCB-183, PCB-167, PCB-174, PCB-177, PCB-156, PCB-172, PCB-180, PCB-170, PCB-201, PCB-203

Only seven participants (3%) ate fish from the Hudson River and only two persons (1%) ate fish from the river after 1994. Thirty individuals (13%) reported consuming fish from Lakes Ontario or Champlain, and 85 persons (36%) ate fish from other fresh bodies of water in New York. Combining these data yielded a total of 92 persons who ate a median of 47 fresh water fish meals over 25 years. Table VI gives the results of the multiple regression analysis of current serum PCB concentrations (log adjusted, lipid basis) on total cumulative fresh water fish consumption when the medium and high consumers (defined as above or below the median value) were compared to non-consumers. In contrast to occupational exposure, there were no significant differences among the fish consumption groups for either light or heavy PCBs or for individual congeners, demonstrating that the PCB body burden, including the congener makeup, reflected occupational and not recreational exposure to PCBs.

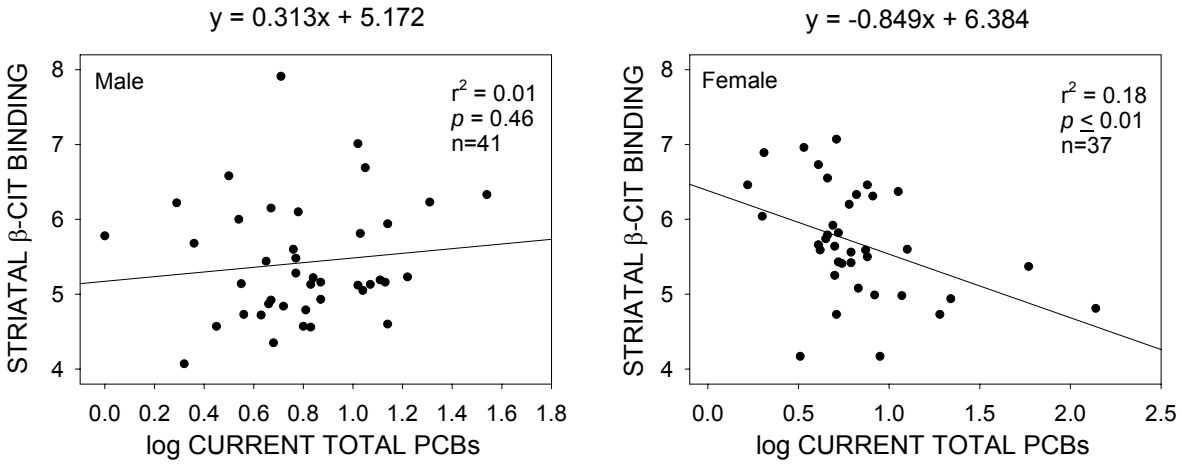
Table VI. Multiple Regression Analysis of current serum PCB concentration (log adjusted, lipid basis) on fresh water fish consumption (N=233)

Serum PCB Concentration (ppm)	Fish Consumption*					
	Medium			High		
	b§	p-value	R^2	b§	p-value	R^2
Light PCBs¥	0.015	0.845	0.00	-0.072	0.084	0.02
Occupational Light PCBs	-0.001	0.994	0.00	-0.083	0.119	0.01
PCB-28	0.091	0.819	0.00	-0.177	0.380	0.00
PCB-74	-0.012	0.968	0.00	-0.206	0.186	0.01
Non-Occupational Light PCBs	0.003	0.984	0.00	-0.132	0.154	0.01
Heavy PCBs#	-0.026	0.592	0.00	-0.008	0.758	0.00
Occupational Heavy PCBs	0.048	0.510	0.00	-0.023	0.525	0.00
PCB-105	0.110	0.775	0.00	-0.004	0.986	0.00
PCB-118	0.080	0.766	0.00	-0.164	0.260	0.01
PCB-156	-0.129	0.546	0.00	-0.016	0.885	0.00
Non-Occupational Heavy PCBs	-0.035	0.747	0.00	-0.003	0.956	0.00
Total PCBs	-0.013	0.823	0.00	-0.031	0.304	0.01

§ Adjusted for age, gender, education, and BMI
* Fish consumption defined as total number of fish meals from selected bodies of fresh water in New York State. Reference group: no fish meals (N=141); medium (N=46) and high (N=46) groups defined according to median split among those who had at least one fish meal
¥ Elute before DDE: PCB-28, PCB-74, PCB-66, PCB-56, PCB-101, PCB-99
Elute after DDE: PCB-118, PCB-146, PCB-153, PCB-105, PCB-138, PCB-178, PCB-187, PCB-183, PCB-167, PCB-174, PCB-177, PCB-156, PCB-172, PCB-180, PCB-170, PCB-201, PCB-203

We now report that the significant statistical relationship between dopamine transporter density, measured by β-CIT SPECT imaging, and current serum total PCB concentrations, observed only in female former capacitor workers is not altered after controlling for potential confounders (age, body mass index, smoking, alcohol consumption, caffeine consumption, bone lead density and the use of cardiovascular medicines). PCB levels were measured in serum from the subjects at the time of imaging. This data, presented in Figure 1, represents the average uptake of the radio-labeled ligand [^{123}I]β-CIT in the putamen and caudate of male and female former exposed workers measured by SPECT imaging, providing an *in*-vivo measure of dopamine transporter density. These data, suggesting a greater susceptibility of women to neurological changes associated with PCB exposure, are supported by the finding of Steenland *et al.* (*Epidemiology* **17**(1), 8-13, 2006) who reported greater Parkinson's disease mortality in women from the same cohort. Most interestingly, recent findings by Lin *et al.* (*Environmental Health Perspectives* **116**(2), 184-189, 2008) also support a gender difference in susceptibility to halogenated hydrocarbons. These authors reported cognitive deficits only in women, but not in men who had been exposed to contaminated rice oil that contained PCBs and dibenzofurans.

Figure 1. Dopamine Transporter Density Measured by β-CIT SPECT Imaging as a function of Current Serum PCB Concentrations



KEY RESEARCH ACCOMPLISHMENTS

As in all epidemiological studies, presentation of results prior to controlling for potential confounders (*e.g.,* age, gender, life style [smoking, alcohol and drug use], and medications) that may affect the dependent variables of interest is premature. We present in Tables I – VI, a significant portion of the material, the data and results from our first manuscript "An Epidemiological Study of Occupational Exposure to PCBs: General Methodologies and Vectors of Exposure" which is in its final draft before submission to *Environmental Health Perspectives.* We also report in Figure 1 that the significant statistical relationship between dopamine transporter density, measured by β-CIT SPECT imaging, and current serum total PCB concentrations which is observed only in female former capacitor workers is not altered after controlling for potential confounders (age, body mass index, smoking, alcohol consumption, caffeine consumption, bone lead density and the use of cardiovascular medicines). Similar statistical analyses are currently being conducted to analyze the relationships between exposure to PCBs and other major dependent variables.

REPORTABLE OUTCOMES

During the past year I have presented findings from this study in two invited plenary lectures: the first at the Collaborative Centers for Parkinson's Disease Environmental Research sponsored by The Parkinson's Institute (Asilomar, CA; April 2007); and the second at the plenary session 'Modifiers of Disease Development in Parkinson's Disease: Role of Environmental Toxicants' 24th International Neurotoxicology Conference (San Antonio, TX; November 2007). In April 2007 I presented a seminar at the Emory University School of Medicine, Center for Neurodegenerative Disease in Atlanta, GA entitled 'Polychlorinated Biphenyl-Induced Neurotoxicity: Relevance to PD' and in October 2007 I presented at seminar at the Stratton VA Medical Center in Albany, NY entitled 'Polychlorinated Biphenyl Neurotoxicity: Relevance to PD'. In addition, I was an invited participant the Parkinson's Institute's Scientific Consensus Conference 'Parkinson's Disease and the Environment' (Sunnyvale, CA; June 2007).

We anticipate a series of five publications summarizing the major findings of the project. Our first manuscript "An Epidemiological Study of Occupational Exposure to PCBs: General Methodologies and Vectors of Exposure," in its final draft before submission to *Environmental Health Perspectives*, describes the associations between serum PCB concentrations and occupational exposure as well as fish consumption; the senior author of this manuscript is Dr. Edward Fitzgerald.

The second manuscript will report on the unexpected statistically significant finding of gender differences in the relationship between dopamine transporter density, measured by β-CIT SPECT imaging, and current serum total PCB concentrations which is observed only in female former capacitor workers

The third manuscript will focus on whether current serum PCB levels can be used to accurately predict concentrations in 1976, using half-life models developed from the subset of study participants who had serum PCB determinations at both time points. The models derived from this analysis would then be used to estimate 1976 PCB body burdens for the entire study population. The writing of this manuscript will be headed by Drs. Seegal and Wolff.

Two additional publications will address the association between both current and estimated historical serum PCB levels and the major health endpoints of the study (1) neurological and (2) neuropsychological measures. We anticipate that the appropriate co-investigators will serve as senior authors for these manuscripts.

CONCLUSIONS

We have come very close to our originally stated goals for recruiting and testing subjects, both in Albany, NY and in New Haven, CT and are proud of this progress since many of our subjects are elderly and must travel considerable distances to undergo testing at these two sites.

The significant negative relationship seen only in female workers—all who were postmenopausal—has allowed us to formulate a hypothesis that estrogen withdrawal increases risk of basal ganglia dopamine dysfunction only in women. This unexpected finding is supported by a recent publication by Steenland *et al.* (*Epidemiology* **17**(1), 8-13, 2006) that demonstrated increased Parkinson's disease mortality only in female former capacitor workers and supports our original hypothesis that, in a manner similar to that seen in PCB-exposed adult non-human primates, PCBs reduce dopamine function in the basal ganglia. Indeed, these findings led to the successful awarding of an NIH grant to Seegal to study the role of gender and ovarian hormones in influencing PCB-induced changes in brain dopamine function. We continue to show that current serum PCB levels are significantly elevated in former capacitor workers compared to literature values for non-occupationally exposed individuals. There are two major findings evident from the analyses of current serum PCB concentrations in this cohort of former capacitor workers.

First, current serum PCB concentrations were significantly associated with cumulative years of occupational exposure with the associations stronger for the occupational congeners than the non-occupational congeners, confirming that congeners such as PCB-74, 105 118, and 156 are indeed unique markers of exposure in this cohort. In addition, the associations with the occupational light congeners were strongest for exposure during the years that Aroclor 1016 were used, whereas the associations with exposure to Aroclor 1242 were similar for both light and heavy occupational congeners. These findings probably reflect that the fact that Aroclor 1016 is comprised mostly of light congeners while 1242 is mixture of both light and heavy congeners. In contrast to the results for occupational exposure, serum PCB concentrations were not associated with the reported consumption of fish from bodies of fresh water in New York State. The lack of an effect for fish consumption may reflect the fact that relatively few persons in this cohort ate fish from the Hudson River and Lakes Ontario and Champlain, the most heavily contaminated bodies of water in New York State. The results nevertheless confirm that the major source of PCB exposure in this cohort is occupational.

The second major finding regarding current PCB concentrations is that the mean levels were approximately three-fold higher in these former capacitor workers than in individuals of similar age who resided in the same towns but did not work at GE. This latter finding—that PCB levels remain elevated more than thirty years after the last direct occupational exposure to PCBs occurred—testifies to the high level of exposure that had occurred in those plants and the long half life of many PCB congeners.

APPENDIX

Invited Meetings and Presentations

'Polychlorinated Biphenyl-Induced Neurotoxicity: Relevance to PD'. Invited plenary lecture speaker at the annual meeting of the Collaborative Centers for Parkinson's Disease Environmental Research sponsored by The Parkinson's Institute; Asilomar, CA, April 2007.

'Polychlorinated Biphenyl-Induced Neurotoxicity: Relevance to PD'. Invited seminar speaker at Emory University School of Medicine, Center for Neurodegenerative Disease, Atlanta, GA, April 2007.

Invited participant at the Parkinson's Institute's Scientific Consensus Conference 'Parkinson's Disease and the Environment', Sunnyvale, CA, June 2007.

'Polychlorinated Biphenyl Neurotoxicity: Relevance to PD'. Invited seminar speaker at the Stratton VA Medical Center, Albany, NY, October 2007.

'The Influence of Gender and Aging on the Effects of Environmental Toxicants in Parkinson's Disease'. Invited speaker in plenary session 'Modifiers of Disease Development in Parkinson's Disease: Role of Environmental Toxicants' 24th International Neurotoxicology Conference, San Antonio, TX, November 2007.